

SEQUENCE LISTING

<110> Cheever, Martin A.
Gheysen, Dirk
Corixa Corporation
SmithKline Beecham Biologicals S. A.

<120> HER-2/neu Fusion Proteins

<130> 014058-009810PC

<140> US 09/493,480
<141> 2000-01-28

<150> US 60/117,976
<151> 1999-01-29

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<170> PatentIn Ver. 2.1

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<212> PRT
<213> Homo sapiens

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<223> extracellular domain (ECD)

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<223> fragment of the phosphorylation domain, preferred
portion (delta PD)

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Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45

Express Mail No.
EL 827035155 US

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
 50 55 60
 Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
 115 120 125
 Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
 130 135 140
 Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
 145 150 155 160
 Leu Cys Tyr Gln Asp Thr-Ile Leu Trp Lys Asp Ile Phe His Lys Asn
 165 170 175
 Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
 180 185 190
 His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
 195 200 205
 Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
 210 215 220
 Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
 225 230 235 240
 Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
 245 250 255
 His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
 260 265 270
 Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
 275 280 285
 Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
 290 295 300
 Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
 305 310 315 320
 Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
 325 330 335
 Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
 340 345 350
 Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
 355 360 365

Arg	Leu	Leu	Gln	Glu	Thr	Glu	Leu	Val	Glu	Pro	Leu	Thr	Pro	Ser	Gly	690	695	700	
Ala	Met	Pro	Asn	Gln	Ala	Gln	Met	Arg	Ile	Leu	Lys	Glu	Thr	Glu	Leu	705	710	715	720
Arg	Lys	Val	Lys	Val	Leu	Gly	Ser	Gly	Ala	Phe	Gly	Thr	Val	Tyr	Lys	725	730	735	
Gly	Ile	Trp	Ile	Pro	Asp	Gly	Glu	Asn	Val	Lys	Ile	Pro	Val	Ala	Ile	740	745	750	
Lys	Val	Leu	Arg	Glu	Asn	Thr	Ser	Pro	Lys	Ala	Asn	Lys	Glu	Ile	Leu	755	760	765	
Asp	Glu	Ala	Tyr	Val	Met	Ala	Gly	Val	Gly	Ser	Pro	Tyr	Val	Ser	Arg	770	775	780	
Leu	Leu	Gly	Ile	Cys	Leu	Thr	Ser	Thr	Val	Gln	Leu	Val	Thr	Gln	Leu	785	790	795	800
Met	Pro	Tyr	Gly	Cys	Leu	Leu	Asp	His	Val	Arg	Glu	Asn	Arg	Gly	Arg	805	810	815	
Leu	Gly	Ser	Gln	Asp	Leu	Leu	Asn	Trp	Cys	Met	Gln	Ile	Ala	Lys	Gly	820	825	830	
Met	Ser	Tyr	Leu	Glu	Asp	Val	Arg	Leu	Val	His	Arg	Asp	Leu	Ala	Ala	835	840	845	
Arg	Asn	Val	Leu	Val	Lys	Ser	Pro	Asn	His	Val	Lys	Ile	Thr	Asp	Phe	850	855	860	
Gly	Leu	Ala	Arg	Leu	Leu	Asp	Ile	Asp	Glu	Thr	Glu	Tyr	His	Ala	Asp	865	870	875	880
Gly	Gly	Lys	Val	Pro	Ile	Lys	Trp	Met	Ala	Leu	Glu	Ser	Ile	Leu	Arg	885	890	895	
Arg	Arg	Phe	Thr	His	Gln	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Val	Thr	Val	900	905	910	
Trp	Glu	Leu	Met	Thr	Phe	Gly	Ala	Lys	Pro	Tyr	Asp	Gly	Ile	Pro	Ala	915	920	925	
Arg	Glu	Ile	Pro	Asp	Leu	Leu	Glu	Lys	Gly	Glu	Arg	Leu	Pro	Gln	Pro	930	935	940	
Pro	Ile	Cys	Thr	Ile	Asp	Val	Tyr	Met	Ile	Met	Val	Lys	Cys	Trp	Met	945	950	955	960
Ile	Asp	Ser	Glu	Cys	Arg	Pro	Arg	Phe	Arg	Glu	Leu	Val	Ser	Glu	Phe	965	970	975	
Ser	Arg	Met	Ala	Arg	Asp	Pro	Gln	Arg	Phe	Val	Val	Ile	Gln	Asn	Glu	980	985	990	
Asp	Leu	Gly	Pro	Ala	Ser	Pro	Leu	Asp	Ser	Thr	Phe	Tyr	Arg	Ser	Leu	995	1000	1005	

Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu Glu Tyr Leu
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Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro Gly Ala Gly
1025 1030 1035 1040

Gly Met Val His His Arg His Arg Ser Ser Ser Thr Arg Ser Gly Gly
1045 1050 1055

Gly Asp Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Ala Pro Arg
1060 1065 1070

Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp Gly
1075 1080 1085

Asp Leu Gly Met Gly Ala Ala Lys Gly Leu Gln Ser Leu Pro Thr His
1090 1095 1100

Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Val Pro Leu
1105 1110 1115 1120

Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys Ser Pro Gln
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Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro Pro Ser Pro
1140 1145 1150

Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala Thr Leu Glu
1155 1160 1165

Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp Val
1170 1175 1180

Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Thr Pro Gln
1185 1190 1195 1200

Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe Ser Pro Ala
1205 1210 1215

Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu Arg Gly Ala
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Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn Pro Glu Tyr
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Leu Gly Leu Asp Val Pro Val
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<211> 1256

<212> PRT

<213> Rattus sp.

<220>

<223> rat HER-2/neu protein

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<221> DOMAIN

<222> (1)..(654)

<223> extracellular domain (ECD)

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B

[illegible][illegible]

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Cys	Ala	Arg	Cys	Lys	Gly	Arg	Leu	Pro	Thr	Asp	Cys	Cys	His	Glu	Gln
225					230					235					240
Cys	Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys
				245					250					255	
Leu	His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu
			260					265					270		
Val	Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	His	Asn	Pro	Glu	Gly
		275					280					285			
Arg	Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Thr	Cys	Pro	Tyr	Asn	Tyr
	290					295					300				
Leu	Ser	Thr	Glu	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Pro	Asn	Asn
305					310					315					320
Gln	Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser
				325					330					335	
Lys	Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg
			340					345					350		
Gly	Ala	Arg	Ala	Ile	Thr	Ser	Asp	Asn	Val	Gln	Glu	Phe	Asp	Gly	Cys
		355					360					365			
Lys	Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly
	370					375					380				
Asp	Pro	Ser	Ser	Gly	Ile	Ala	Pro	Leu	Arg	Pro	Glu	Gln	Leu	Gln	Val
385				390						395					400
Phe	Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp
			405						410					415	
Pro	Asp	Ser	Leu	Arg	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Arg	Ile	Ile
			420					425					430		
Arg	Gly	Arg	Ile	Leu	His	Asp	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly
		435					440					445			
Leu	Gly	Ile	His	Ser	Leu	Gly	Leu	Arg	Ser	Leu	Arg	Glu	Leu	Gly	Ser
	450					455					460				
Gly	Leu	Ala	Leu	Ile	His	Arg	Asn	Ala	His	Leu	Cys	Phe	Val	His	Thr
465					470					475					480
Val	Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His
				485					490					495	
Ser	Gly	Asn	Arg	Pro	Glu	Glu	Asp	Cys	Gly	Leu	Glu	Gly	Leu	Val	Cys
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Cys Val Asn Cys Ser His Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
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 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Ser Asp Lys Arg
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 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
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 Cys Phe Gly Ser Glu Ala Asp Gln Cys Ala Ala Cys Ala His Tyr Lys
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 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
 610 615 620
 Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
 625 630 635 640
 Arg Gly Cys Pro Ala Glu-Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
 645 650 655
 Ala Thr Val Glu Gly Val Leu Leu Phe Leu Ile Leu Val Val Val Val
 660 665 670
 Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
 675 680 685
 Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
 690 695 700
 Gly Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu
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 Leu Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr
 725 730 735
 Lys Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala
 740 745 750
 Ile Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile
 755 760 765
 Leu Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser
 770 775 780
 Arg Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln
 785 790 795 800
 Leu Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu His Arg Gly
 805 810 815
 Arg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Val Gln Ile Ala Lys
 820 825 830
 Gly Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala
 835 840 845

106050-9524360

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His	Pro	Cys	Ser	Pro	Met	Cys	Lys	Gly	Ser	Arg	Cys	Trp	Gly	Glu	Ser	
		195					200					205				
Ser	Glu	Asp	Cys	Gln	Ser	Leu	Thr	Arg	Thr	Val	Cys	Ala	Gly	Gly	Cys	
	210					215					220					
Ala	Arg	Cys	Lys	Gly	Pro	Leu	Pro	Thr	Asp	Cys	Cys	His	Glu	Gln	Cys	
225					230					235					240	
Ala	Ala	Gly	Cys	Thr	Gly	Pro	Lys	His	Ser	Asp	Cys	Leu	Ala	Cys	Leu	
				245					250					255		
His	Phe	Asn	His	Ser	Gly	Ile	Cys	Glu	Leu	His	Cys	Pro	Ala	Leu	Val	
			260					265						270		
Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	Pro	Asn	Pro	Glu	Gly	Arg	
		275					280					285				
Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Ala	Cys	Pro	Tyr	Asn	Tyr	Leu	
	290					295					300					
Ser	Thr	Asp	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Leu	His	Asn	Gln	
305					310					315					320	
Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser	Lys	
			325						330					335		
Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg	Glu	
			340					345						350		
Val	Arg	Ala	Val	Thr	Ser	Ala	Asn	Ile	Gln	Glu	Phe	Ala	Gly	Cys	Lys	
		355					360					365				
Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly	Asp	
	370					375					380					
Pro	Ala	Ser	Asn	Thr	Ala	Pro	Leu	Gln	Pro	Glu	Gln	Leu	Gln	Val	Phe	
385					390					395					400	
Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp	Pro	
			405						410					415		
Asp	Ser	Leu	Pro	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Gln	Val	Ile	Arg	
			420					425						430		
Gly	Arg	Ile	Leu	His	Asn	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly	Leu	
		435					440						445			
Gly	Ile	Ser	Trp	Leu	Gly	Leu	Arg	Ser	Leu	Arg	Glu	Leu	Gly	Ser	Gly	
	450					455					460					
Leu	Ala	Leu	Ile	His	His	Asn	Thr	His	Leu	Cys	Phe	Val	His	Thr	Val	
465					470					475					480	
Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His	Thr	
				485					490					495		

Pro Thr His Asp Pro Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr
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Val Pro Leu Pro Ser Glu Thr Asp Gly Tyr Val Ala Pro Leu Thr Cys
130 135 140

Ser Pro Gln Pro Glu Tyr Val Asn Gln Pro Asp Val Arg Pro Gln Pro
145 150 155 160

Pro Ser Pro Arg Glu Gly Pro Leu Pro Ala Ala Arg Pro Ala Gly Ala
165 170 175

Thr Leu Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val
180 185 190

Lys Asp Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu
195 200 205

Thr Pro Gln Gly Gly Ala Ala Pro Gln Pro His Pro Pro Pro Ala Phe
210 215 220

Ser Pro Ala Phe Asp Asn-Leu Tyr Tyr Trp Asp Gln Asp Pro Pro Glu
225 230 235 240

Arg Gly Ala Pro Pro Ser Thr Phe Lys Gly Thr Pro Thr Ala Glu Asn
245 250 255

Pro Glu Tyr Leu Gly Leu Asp Val Pro Val
260 265

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<211> 59

<212> PRT

<213> Homo sapiens

<220>

<223> fragment of the phosphorylation domain, preferred
portion (delta PD) of human HER-2/neu

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Gln Asn Glu Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr
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Arg Ser Leu Leu Glu Asp Asp Asp Met Gly Asp Leu Val Asp Ala Glu
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Glu Tyr Leu Val Pro Gln Gln Gly Phe Phe Cys Pro Asp Pro Ala Pro
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Gly Ala Gly Gly Met Val His His Arg His Arg
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<210> 6

<211> 919

<212> PRT

<213> Artificial Sequence

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<223> Description of Artificial Sequence: fusion protein
of ECD and PD of human HER-2/neu

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20 25 30
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35 40 45
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50 55 60
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65 70 75 80
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85 90 95
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100 105 110
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115 120 125
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130 135 140
Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145 150 155 160
Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165 170 175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180 185 190
His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195 200 205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210 215 220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225 230 235 240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245 250 255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260 265 270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275 280 285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290 295 300

000050-9554550

Ser	Thr	Asp	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Leu	His	Asn	Gln	305	310	315	320
Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser	Lys	325	330	335	
Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg	Glu	340	345	350	
Val	Arg	Ala	Val	Thr	Ser	Ala	Asn	Ile	Gln	Glu	Phe	Ala	Gly	Cys	Lys	355	360	365	
Lys	Ile	Phe	Gly	Ser	Leu	Ala	Phe	Leu	Pro	Glu	Ser	Phe	Asp	Gly	Asp	370	375	380	
Pro	Ala	Ser	Asn	Thr	Ala	Pro	Leu	Gln	Pro	Glu	Gln	Leu	Gln	Val	Phe	385	390	395	400
Glu	Thr	Leu	Glu	Glu	Ile	Thr	Gly	Tyr	Leu	Tyr	Ile	Ser	Ala	Trp	Pro	405	410	415	
Asp	Ser	Leu	Pro	Asp	Leu	Ser	Val	Phe	Gln	Asn	Leu	Gln	Val	Ile	Arg	420	425	430	
Gly	Arg	Ile	Leu	His	Asn	Gly	Ala	Tyr	Ser	Leu	Thr	Leu	Gln	Gly	Leu	435	440	445	
Gly	Ile	Ser	Trp	Leu	Gly	Leu	Arg	Ser	Leu	Arg	Glu	Leu	Gly	Ser	Gly	450	455	460	
Leu	Ala	Leu	Ile	His	His	Asn	Thr	His	Leu	Cys	Phe	Val	His	Thr	Val	465	470	475	480
Pro	Trp	Asp	Gln	Leu	Phe	Arg	Asn	Pro	His	Gln	Ala	Leu	Leu	His	Thr	485	490	495	
Ala	Asn	Arg	Pro	Glu	Asp	Glu	Cys	Val	Gly	Glu	Gly	Leu	Ala	Cys	His	500	505	510	
Gln	Leu	Cys	Ala	Arg	Gly	His	Cys	Trp	Gly	Pro	Gly	Pro	Thr	Gln	Cys	515	520	525	
Val	Asn	Cys	Ser	Gln	Phe	Leu	Arg	Gly	Gln	Glu	Cys	Val	Glu	Glu	Cys	530	535	540	
Arg	Val	Leu	Gln	Gly	Leu	Pro	Arg	Glu	Tyr	Val	Asn	Ala	Arg	His	Cys	545	550	555	560
Leu	Pro	Cys	His	Pro	Glu	Cys	Gln	Pro	Gln	Asn	Gly	Ser	Val	Thr	Cys	565	570	575	
Phe	Gly	Pro	Glu	Ala	Asp	Gln	Cys	Val	Ala	Cys	Ala	His	Tyr	Lys	Asp	580	585	590	
Pro	Pro	Phe	Cys	Val	Ala	Arg	Cys	Pro	Ser	Gly	Val	Lys	Pro	Asp	Leu	595	600	605	
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 <212> PRT
 <213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: fusion protein
 of ECD and delta PD of human HER-2/neu

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Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
      20              25              30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
      35              40              45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
      50              55              60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
      65              70              75              80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
      85              90              95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
      100             105             110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
      115             120             125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
      130             135             140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
      145             150             155             160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
      165             170             175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
      180             185             190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
      195             200             205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
      210             215             220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
      225             230             235             240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
      245             250             255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
      260             265             270

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000050-9545860

Thr	Tyr	Asn	Thr	Asp	Thr	Phe	Glu	Ser	Met	Pro	Asn	Pro	Glu	Gly	Arg		
		275					280						285				
Tyr	Thr	Phe	Gly	Ala	Ser	Cys	Val	Thr	Ala	Cys	Pro	Tyr	Asn	Tyr	Leu		
	290					295					300						
Ser	Thr	Asp	Val	Gly	Ser	Cys	Thr	Leu	Val	Cys	Pro	Leu	His	Asn	Gln		
305					310					315					320		
Glu	Val	Thr	Ala	Glu	Asp	Gly	Thr	Gln	Arg	Cys	Glu	Lys	Cys	Ser	Lys		
				325					330						335		
Pro	Cys	Ala	Arg	Val	Cys	Tyr	Gly	Leu	Gly	Met	Glu	His	Leu	Arg	Glu		
			340					345					350				
Val	Arg	Ala	Val	Thr	Ser	Ala	Asn	Ile	Gln	Glu	Phe	Ala	Gly	Cys	Lys		
	355						360					365					
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 gatgggggca aggtgcccac caagtggatg caatttggaat ctattctcag acgccgggtc 2700
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 gccaaacctt acgatgggat cccagctcgg gagatccctg atttgctgga gaagggagaa 2820
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[illegible]

Leu Pro Ala Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
 65 70 75 80
 Gln Gly Tyr Met Leu Ile Ala His Asn Arg Val Lys His Val Pro Leu
 85 90 95
 Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr
 100 105 110
 Ala Leu Ala Val Leu Asp Asn Arg Asp Pro Leu Asp Asn Val Thr Thr
 115 120 125
 Ala Ala Pro Gly Arg Thr Pro Glu Gly Leu Arg Glu Leu Gln Leu Arg
 130 135 140
 Ser Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Arg Gly Asn Pro
 145 150 155 160
 Gln Leu Cys Tyr Gln Asp Met Val Leu Trp Lys Asp Val Leu Arg Lys
 165 170 175
 Asn Asn Gln Leu Ala Pro Val Asp Met Asp Thr Asn Arg Ser Arg Ala
 180 185 190
 Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu
 195 200 205
 Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly
 210 215 220
 Cys Ala Arg Cys Lys Gly Arg Leu Pro Thr Asp Cys Cys His Glu Gln
 225 230 235 240
 Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys
 245 250 255
 Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
 260 265 270
 Ile Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Leu Asn Pro Glu Gly
 275 280 285
 Arg Tyr Thr Phe Gly Ala Ser Cys Val Thr Thr Cys Pro Tyr Asn Tyr
 290 295 300
 Leu Ser Thr Glu Val Gly Ser Cys Thr Leu Val Cys Pro Pro Asn Asn
 305 310 315 320
 Gln Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser
 325 330 335
 Lys Pro Cys Ala Gly Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg
 340 345 350
 Gly Ala Arg Ala Ile Thr Ser Asp Asn Ile Gln Glu Phe Ala Gly Cys
 355 360 365
 Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly
 370 375 380

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Asn Pro Ser Ser Gly Val Ala Pro Leu Lys Pro Glu His Leu Gln Val
 385 390 395 400
 Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp
 405 410 415
 Pro Glu Ser Phe Gln Asp Leu Ser Val Phe Gln Asn Leu Arg Val Ile
 420 425 430
 Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
 435 440 445
 Leu Gly Ile His Ser Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser
 450 455 460
 Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
 465 470 475 480
 Val Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His
 485 490 495
 Ser Gly Asn Arg Pro Glu Glu Ala Cys Gly Leu Glu Gly Leu Val Cys
 500 505 510
 Asn Ser Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln
 515 520 525
 Cys Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu
 530 535 540
 Cys Arg Val Trp Lys Gly Leu Pro Arg Glu Tyr Val Arg Gly Lys His
 545 550 555 560
 Cys Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Ser Ser Glu Thr
 565 570 575
 Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
 580 585 590
 Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
 595 600 605
 Leu Ser Tyr Met Pro Ile Trp Lys Tyr Pro Asp Glu Glu Gly Ile Cys
 610 615 620
 Gln Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Glu
 625 630 635 640
 Arg Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Val Thr Phe Ile Ile
 645 650 655
 Ala Thr Val Val Gly Val Leu Leu Phe Leu Ile Ile Val Val Val Ile
 660 665 670
 Gly Ile Leu Ile Lys Arg Arg Arg Gln Lys Ile Arg Lys Tyr Thr Met
 675 680 685
 Arg Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser
 690 695 700

Gly	Ala	Val	Pro	Asn	Gln	Ala	Gln	Met	Arg	Ile	Leu	Lys	Glu	Thr	Glu	
705					710					715					720	
Leu	Arg	Lys	Leu	Lys	Val	Leu	Gly	Ser	Gly	Ala	Phe	Gly	Thr	Val	Tyr	
				725					730						735	
Lys	Gly	Ile	Trp	Ile	Pro	Asp	Gly	Glu	Asn	Val	Lys	Ile	Pro	Val	Ala	
			740					745						750		
Ile	Lys	Val	Leu	Arg	Glu	Asn	Thr	Ser	Pro	Lys	Ala	Asn	Lys	Glu	Ile	
		755					760					765				
Leu	Asp	Glu	Ala	Tyr	Val	Met	Ala	Gly	Val	Gly	Ser	Pro	Tyr	Val	Ser	
	770					775					780					
Arg	Leu	Leu	Gly	Ile	Cys	Leu	Thr	Ser	Thr	Val	Gln	Leu	Val	Thr	Gln	
785					790					795					800	
Leu	Met	Pro	Tyr	Gly	Cys	Leu	Leu	Asp	His	Val	Arg	Glu	His	Arg	Gly	
				805					810					815		
Arg	Leu	Gly	Ser	Gln	Asp	Leu	Leu	Asn	Trp	Cys	Val	Gln	Ile	Ala	Lys	
			820					825						830		
Gly	Met	Ser	Tyr	Leu	Glu	Glu	Val	Arg	Leu	Val	His	Arg	Asp	Leu	Ala	
		835					840					845				
Ala	Arg	Asn	Val	Leu	Val	Lys	Ser	Pro	Asn	His	Val	Lys	Ile	Thr	Asp	
	850					855					860					
Phe	Gly	Leu	Ala	Arg	Leu	Leu	Asp	Ile	Asp	Glu	Thr	Glu	Tyr	His	Ala	
865					870					875					880	
Asp	Gly	Gly	Lys	Val	Pro	Ile	Lys	Trp	Met	Ala	Leu	Glu	Ser	Ile	Leu	
			885						890					895		
Arg	Arg	Arg	Phe	Thr	His	Gln	Ser	Asp	Val	Trp	Ser	Tyr	Gly	Val	Thr	
			900					905					910			
Val	Trp	Glu	Leu	Met	Thr	Phe	Gly	Ala	Lys	Pro	Tyr	Asp	Gly	Ile	Pro	
		915					920						925			
Ala	Arg	Glu	Ile	Pro	Asp	Leu	Leu	Glu	Lys	Gly	Glu	Arg	Leu	Pro	Gln	
	930					935					940					
Pro	Pro	Ile	Cys	Thr	Ile	Asp	Val	Tyr	Met	Ile	Met	Val	Lys	Cys	Trp	
945					950					955					960	
Met	Ile	Asp	Ser	Glu	Cys	Arg	Pro	Arg	Phe	Arg	Glu	Leu	Val	Ser	Glu	
			965						970					975		
Phe	Ser	Arg	Met	Ala	Arg	Asp	Pro	Gln	Arg	Phe	Val	Val	Ile	Gln	Asn	
			980					985					990			
Glu	Asp	Leu	Gly	Pro	Ser	Ser	Pro	Met	Asp	Ser	Thr	Phe	Tyr	Arg	Ser	
		995					1000					1005				
Leu	Leu	Glu	Asp	Asp	Asp	Met	Gly	Glu	Leu	Val	Asp	Ala	Glu	Glu	Tyr	
	1010					1015					1020					

Leu Val Pro Gln Gln Gly Phe Phe Ser Pro Asp Pro Ala Leu Gly Thr
 1025 1030 1035 1040
 Gly Ser Thr Ala His Arg Arg His Arg Ser Ser Ser Ala Arg Ser Gly
 1045 1050 1055
 Gly Gly Glu Leu Thr Leu Gly Leu Glu Pro Ser Glu Glu Glu Pro Pro
 1060 1065 1070
 Arg Ser Pro Leu Ala Pro Ser Glu Gly Ala Gly Ser Asp Val Phe Asp
 1075 1080 1085
 Gly Asp Leu Ala Val Gly Val Thr Lys Gly Leu Gln Ser Leu Ser Pro
 1090 1095 1100
 His Asp Leu Ser Pro Leu Gln Arg Tyr Ser Glu Asp Pro Thr Leu Pro
 1105 1110 1115 1120
 Leu Pro Pro Glu Thr Asp Gly Tyr Val Ala Pro Leu Ala Cys Ser Pro
 1125 1130 1135
 Gln Pro Glu Tyr Val Asn Gln Pro Glu Val Arg Pro Gln Ser Pro Leu
 1140 1145 1150
 Thr Pro Glu Gly Pro Pro Pro Pro Ile Arg Pro Ala Gly Ala Thr Leu
 1155 1160 1165
 Glu Arg Pro Lys Thr Leu Ser Pro Gly Lys Asn Gly Val Val Lys Asp
 1170 1175 1180
 Val Phe Ala Phe Gly Gly Ala Val Glu Asn Pro Glu Tyr Leu Ala Pro
 1185 1190 1195 1200
 Arg Ala Gly Thr Ala Ser Gln Pro His Pro Ser Pro Ala Phe Ser Pro
 1205 1210 1215
 Ala Phe Asp Asn Leu Tyr Tyr Trp Asp Gln Asn Ser Ser Glu Gln Gly
 1220 1225 1230
 Pro Pro Pro Ser Thr Phe Glu Gly Thr Pro Thr Ala Glu Asn Pro Glu
 1235 1240 1245
 Tyr Leu Gly Leu Asp Val Pro Val
 1250 1255

<210> 15

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-251

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32

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<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:PCR primer
PDM-279

<400> 16
ctggactcga gtcattagcg gtgcctgtgg tgg 33

<210> 17
<211> 32
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW028 hECD-PD
sense primer with NcoI site

<400> 17
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<210> 18
<211> 31
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:AW029 hECD-PD
antisense primer with XhoI site without stop

<400> 18
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<210> 19
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<212> DNA
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<220>

<223> Description of Artificial Sequence:AW038 primer
for site-directed mutagenesis

<400> 19
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<210> 20
<211> 35
<212> DNA
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<220>

<223> Description of Artificial Sequence:AW039 primer
for site-directed mutagenesis

<400> 20
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35

<210> 21
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW036 sense
primer with NcoI site

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28

<210> 22
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:AW037 antisense
primer with XhoI site

<400> 22
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g 61

<210> 23
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC05 PCR
fragment

<400> 23
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33

<210> 24
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Ra12.JC06 PCR
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<400> 24
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29

<210> 25
<211> 30
<212> DNA
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LeIF.JC03 PCR
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30

<210> 26

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:LeIF.JC04 PCR
fragment

<400> 26

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32

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